CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA
RESMETHRIN

Chemical Code # 2119, Tolerance # 50248
SB-950 # 839

October 13, 1987
Revised: 04/13/88, 06/07/88, 11/09/89, 03/28/91, 04/12/92, 02/10/93, 02/21/95, 10/13/95, 03/05/96, 04/03/96, 02/20/97, 8/6/98

I. DATA GAP STATUS

Chronic toxicity, rat:	No data gap, possible adverse effect
Chronic toxicity, dog:	No data gap, possible adverse effect
Oncogenicity, rat:	No data gap, possible adverse effect
Oncogenicity, mouse:	No data gap, possible adverse effect
Reproduction, rat:	No data gap, possible adverse effect
Teratology, rat:	No data gap, no adverse effect
Teratology, rabbit:	No data gap, possible adverse effect
Gene mutation:	No data gap, no adverse effect
Chromosome effects:	No data gap, no adverse effect
DNA damage:	No data gap, no adverse effect
Neurotoxicity:	No study required at this time

Toxicology one-liners are attached.
All record numbers through 150992 and 960767 were examined.
** indicates an acceptable study.
Bold face indicates a possible adverse effect.
indicates additional submissions on file but no yet reviewed.
File name: t980806.wpd
Revised by J. Gee, 8/6/98

Note: EPA's reregistration guidelines for resmethrin is contained in DPR doc. # 50248-083.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

****50248-252; 134161;** "Combined Chronic Toxicity and Oncogenicity Study in Rats with SPB-1382 (Resmethrin) Technical," HWA 2623-104; J.A. Trutter; Hazleton Washington, Inc., Vienna, VA; 2/28/94. Resmethrin technical (SBP-1382, lot No. IN-0837 B3, 85% stated purity) was fed in the diets of 65 Sprague-Dawley rats/sex/group at concentrations of 0, 250, 1000, or 2500 ppm for 24 months. With the possible exception of decreased body weights in 100-week old females and 6% increase in total food consumption for males at 2500 ppm. There were no treatment-related effects on body weight, food consumption, or survival. There were sporadic treatment-related decreases in erythrocyte counts, hemoglobin, and hematocrit at 1000 ppm in males and 2500 ppm in both sexes and total cholesterol in females at 1000 and 2500 ppm (non-oncogenic NOEL = 250 ppm). A **possible adverse effect** was indicated by increases in effects seen in females at 2500 ppm: liver and uterine masses; uterine cysts and polyps; and liver adenomas and carcinomas. The study was unacceptable (S. Morris and J. Kishiyama, 4/3/96) but upgraded by adequacy of dosing being demonstrated by the possible adverse effects (S. Morris and J. Gee, 2/20/97).

> 50248-275; 150992; "Subchronic Toxicity Study in Rats with SBP-1382 (Resmethrin) Technical," HWA 2623-101. This document contained an adequate certificate of analysis and a subchronic rat study in which five groups of 20 Crl:CD®BR rats per sex were fed dietary mixtures of SBP-1382 (Resmethrin) Technical (lot No. IN-0198-B3, 86.3% purity) for at least 13 consecutive weeks at 0, 500, 1250, 2500, 5000, or 10000 ppm. Six females died at 10000 ppm. Treatment-related clinical signs at 10000 ppm in both sexes included hunched posture, urine stains, tremors, hypersensitivity to sound, thin appearance, hypoactivity, poor appetite, few feces, perinatal crust, and/or a nose crusts. Treatment-related clinical signs at 5000 ppm in both sexes included tremors, hunched posture, and/or hypersensitivity to sound. When compared to controls, group mean body weights and body weight gains were decreased at 5000 and 10000 ppm and group mean food consumption was lower at 10000 ppm. Significant treatment-related effects on clinical chemistry were decreased hemoglobin and hematocrit in females at 5000 and 10000 ppm. There were treatment-related decreases in absolute weights for brain, heart, ovary, spleen, kidney, and testis/epididymis and increases for liver and thyroid/parathyroid. Dose-dependent increases in organ/body weight ratios were seen for the previously-mentioned organs. There were treatment-related histological changes in liver and thyroid: hepatocellular vacuolization (1250, 2500, and 5000 ppm) and hypertrophy (1250, 2500, 5000, and 10000 ppm) in both sexes and thyroid follicular cell vacuolization (2500, 5000, 10000 ppm) in females. Evaluation of these data resulted in a change of study status to acceptable for the study at DPR doc. # 50248-252, rec. # 134161. See DPR Worksheet, 2/19/97 (S. Morris and J. Gee, 2/20/97).
>
> Note: The possible oncogenic effects were listed under the chronic and oncogenicity test types.

50248-187; 050147; "A Lifetime Evaluation of the Dietary Administration of SBP-1382 to Wistar

Albino Rats", FDRL # 5271; Food and Drug Research Laboratories, Waverly Research Center; 5/2/80; resmethrin, SBP-1382 technical, 90% purity; Groups of 60 Wistar rats/sex were exposed to nominal dietary concentrations of 0, 500, 2500, or 5000 ppm (analytical concentrations . 356, 1974, 3703 ppm) for up to 2 years. Ten rats/group were selected for interim sacrifices at one year. Although obscured by endemic and geriatric diseases, possibly treatment-related effects included: increased liver weights in females at 1974 and 3703 ppm and in males at 3703 ppm; increased thyroid weights in females at 3703 ppm; decreased spleen weights in females at 1974 and 3703 ppm; increased thyroid cysts in males at 3703 ppm; and increased proliferative liver lesions in females at 1974 and 3703 ppm. There was no evidence of an oncogenic effect. A **possible adverse effect** may be indicated by the proliferative liver lesions and thyroid cysts with a NOEL of 356 ppm. The study status was changed from unacceptable as a combined study (Davis, 9/8/87) to acceptable as an oncogenicity study only (S. Morris, 11/1/89). The study is not acceptable and not upgradeable as a chronic toxicity study because the target organ could not be identified due to the numerous and possibly age and disease-related pathological findings in all organs of all groups.

EPA ONE LINER-NOEL < 500 ppm for any response (minimal hypertrophy of hepatocytes at 500 ppm). NOEL = 500 ppm for toxic response. LEL = 2500 ppm, increases in liver weight & increase in liver pathological lesions, at 5000 ppm increases in thyroid wt. and cysts.

Oncogenic NOEL = 500 ppm, oncogenic LEL = 2500 ppm.
Levels tested = 0, 250 (sic), and 5000 ppm.
CORE Grade Minimum

50248-188; 050148;
50248-189; 050149;
50248-190; 050481;
50248-191; 050482: These documents contain appendices to 50248-187; 050147.
50248-041; 960764: This document contains a partial copy of 50248-187; 050147.

50248-042; 050483;
50248-192; 050483; "Supplemental I Report (Pathology Report)" (10/29/81) Supplemental reevaluation of the thyroid gland histopathology by S. W. Thompson. Negative for thyroid oncogenicity. Davis 9/14/87.

50248-041; 960767; (7/7/82) Review of the effects of resmethrin on the thyroid in this study by C. D. King, a consultant. He concludes that there is no evidence for oncogenicity. Davis 9/16/87.

50248-043; 050492;
50248-194; 050492; "Amendment II. Supplemental Report (Pathology Report)" (10/29/81) Supplemental reevaluation of the liver histopathology by S. W. Thompson. This document contains data that disputed the findings of an oncogenic effect in female liver reported in the original study. Davis 9/14/87.

50248-041; 050145;
50248-186; 050145; "Study Audit Report. SBP-1382 Lifetime Rat Oral Toxicity and Carcinogenic Study (FDRL 5271)" (6/20/80) Audit by C. D. King, a consultant, found several major problems. Davis 9/14/87.

50248-196; 050494; EPA/FDA audit of the study. Davis 9/16/87.

50248-202; 069529: This document contained an acceptable retrospective diet analysis that demonstrated the homogeneity and stability of SBP-1382 technical in animal feed. This study was not sufficient to address the deficiencies in diet analysis in the study at DPR doc. # 50248-187, rec. # 050147. A worksheet was done (Shimer/S. Morris, 09/01/89).

50248-193; 050484;
50248-193; 050485;
50248-193; 050486;
50248-193; 050487;
50248-193; 050488;
50248-193; 050489;
50248-193; 050490;
50248-193; 050491: These documents contain one IRDC report and seven studies from the open literature on spontaneous tumor rates in rats. Critical portions of text are illegible. No worksheets were done (S. Morris, 10/24/89).

50248-203; 069530: This document contains registrant's comments, summary tables of urinalysis data, a cumulative mortality table, and individual daily observation data. A supplemental worksheet was done that changed the study status from unacceptable to acceptable as an oncogenicity study only (S. Morris, 11/1/89).

50248-212; 086957: This document contains copies of previously-submitted data on body weights and compound consumption. No worksheet was done (S. Morris, 02/06/91).

50248-222: This document contains statements about DPR's findings (letter dated 1/9/91). DPR's response (4/12/92) to these statments did not result in a study status change.

CHRONIC TOXICITY, RAT

See Combined, Rat above.

CHRONIC TOXICITY, DOG

****50248-245; 128007;** "52-Week Oral Toxicity Study SBP-1382 (Resmethrin) Technical in Dogs", HWA 2623-105; H.W. Dalgard; Hazleton Washington, Inc., Vienna VA; 11/23/93. Resmethrin Technical (SPB-1382, lot # IN0198-B3, 86.3% state purity) was given orally in gelatin capsules at 0 (empty capsule), 12.5. 125, 500 or 2000 mg/kg/day (not corrected for purity) to 4 beagle dogs/sex/group for 52 weeks. Adequacy of dosing was based on the limit test (2000 mg/kg/day . 6.7% diet). Treatment-related effects included: a decrease in body weight gain in males (weeks 2 -24), increased liver size in both sexes and increased liver hypertrophy and gallbladder vacuolization in males at 2000 mg/kg/day. A **possible adverse effect** was indicated by posterior subcapsular cataracts in males at 500 and 2000 mg/kg/day and decreased erythrocyte count in males at 2000 mg/kg/day and females at 125, 500, and 2000 mg/kg/day (NOEL = 12.5 mg/kg/day). The study was

unacceptable (S. Morris, J. Kishiyama, 4/1/96) but upgraded to acceptable with submission of adequate analytical data for the test material (S. Morris and J Gee, 2/19/97).

Note: On 02/13/92 a telephone conversation took place between Dr. Joyce Gee of DPR and Dr. John DeProspo of Roussel Bio Corporation. They discussed the high dose selection for a replacement one-year dog study based on the results of a 90-day subchronic study conducted at Roussel Bio. Dr Gee's notes of this conversation are on file at DPR.

50248-183; 054201; "180-Day Subchronic Oral Dosing Study with Resmethrin (SBP-1382) in Beagle Dogs", FDRL # 6289; Food and Drug Research Laboratories, Waverly Research Center; 12/18/80; resmethrin, SBP-1382, lot #'s 8147-LBO-1, 8176-RT, 8147-LCO-1, purity unstated; Groups of 6 dogs/sex were dosed p.o. with 0, 10, 30, or 300 (increased from 100 on day 57) mg/kg/day in capsules. Signs of toxicity were seen at 30 and 300 mg/kg: tremors in males and increased liver weights in females (NOEL = 10 mg/kg). No adverse effect was indicated. The study is unacceptable and not upgradeable because of insufficient treatment duration and insufficient toxicity at the highest dose (Davis, 8/20/87, 4/13/88; S. Morris, 10/4/89).

EPA ONE LINER
NOEL = 10 mg/kg/day
LEL = 30 mg/kg/day (increased liver wt. in females)
Levels tested by capsule in beagles-0, 10, 30, 100, [sic] and 300 mg/kg/day

50248-201; 069526: This document contains supplemental information about the lot numbers of the test materials and rationales for the doses used in the study at DPR doc. # 50248-183, rec. # 054201. Evaluation of these data did not result in a change of study status. No worksheet was done (S. Morris, 09/06/89).

50248-083; 076009: This document contains EPA's evaluation of the study at DPR doc. # 50248-183, rec. # 054201. Examination of this evaluation data did not result in a change of study status. No worksheet was done (S. Morris, 10/04/89).
50248-229; 118440: This document contains a summary of the study at DPR doc. # 50248-183, rec. # 054201. No worksheet was done (S. Morris, 3/9/93).

ONCOGENICITY, RAT

See Combined, Rat above.

ONCOGENICITY, MOUSE

50248-181; 054291; "Evaluation of Dietary Administration of SBP-1382 in CD-1 Outbred Albino Mice Over an 85 Week Period" (Food and Drug Research Laboratories, Waverly Research Center, Lab. No. 5270, 6/6/79) Resmethrin (SBP-1382 technical, 90% purity) at 0, 250, 500, or 1000 ppm in the diet to 75 mice/sex/group to evaluate oncogenicity; **NO ADVERSE EFFECT**-NOEL for oncogenicity > 1000 ppm; NOEL for chronic toxicity = 500 ppm (mortality; amyloidosis; elevated adrenal, liver, kidney, and brain weights); **UNACCEPTABLE, CAN'T BE UPGRADED**-inadequate diet analysis, nonrandom distribution of mice into groups, deficient hematology and histopathology; Davis 8/14/87.

EPA ONE LINER-NOEL Oncogenic NOEL > 1000 ppm (HDT)

Levels tested = 0, 250, 500 and 1000 ppm

50248-202; 069529; This document contained an acceptable retrospective diet analysis that demonstrated the homogeneity and stability of SBP-1382 technical in animal feed. This study was not sufficient to address the deficiencies in diet analysis in the study at DPR doc. # 50248-181, rec. # 054291. A worksheet was done (Shimer/S. Morris, 09/01/89).

**** 50248-222; 112345;** "A Dietary Oncogenicity Study of SBP-1382 in the Albino Mouse"; L. Kangas; Bio-Research Laboratories Ltd., Senneville, Quebec, Canada; Laboratory Project ID 83754; 01/08/92; Five groups of 50 Swiss Crl:CD^{R}-1(ICR)BR mice per sex were fed diets containing resmethrin (SBP-1382, lot 8N 0731B3, 84.8% mean analytical purity) at 0, 0, 300, 600, or 1200 ppm. Treatment-related decreased testes weights in males and increased liver and kidney weights in both sexes were seen at 600 and 1200 ppm (nominal NOEL = 300 ppm) and increased diffuse (both sexes) and centrilobular (males) hypertrophy of hepatocytes were seen 1200 ppm. A **possible adverse effect** was indicated by a treatment-related increase in hepatocellular adenomas and carcinomas in the males at 300, 600, and 1200 ppm. There was a compound-related decrease in male survival at 24 months. This effect did not demonstrate an MTD because it was not: significant at 18 months, related to dose, seen in the females, or correlated with clinical or pathology signs. The study is unacceptable but possibly upgradeable with submission of an adequate rationale for the highest dose (S. Morris and J. Gee, 2/25/92). In response to a letter from AgrEvo, dated 4/1/98, the long-term studies in the rat, mouse and dog were reconsidered. The mouse oncogenicity study has been upgraded to acceptable status with a possible adverse effect. See rebuttal R980806 for details. (Gee, 8/6/98)

50248-229; 118422;
50248-229; 118443; "A 4-Week Dietary Toxicity Study of SBP-1382 in the Albino Mouse"; L. Kangas; Bio-Research Laboratories Ltd., Senneville, Quebec, Canada; Laboratory Project ID 83753; 11/27/89. The report was submitted as part of a rationale for the doses used in the study at DPR doc. # 50248-222, rec. # 112345. Evaluation of these data resulted in no change in data gap status. No worksheet was done. See response dated 3/9/93 (S. Morris).

50248-229; 118423: This document contained comments about the rationale for the doses used in the study at DPR doc. # 50248-222, rec. # 112345 and no data. Evaluation of these comments resulted in no change in data gap status. No worksheet was done. See response dated 3/9/93 (S. Morris).

50248-229; 118446: This document contains an analysis of liver tumors by survival time used in the study at DPR doc. # 50248-222, rec. # 112345. Evaluation of these analysis resulted in no change in data gap status. No worksheet was done. See response dated 3/9/93 (S. Morris).

50248-229; 118445;
50248-229; 118447: These documents contain historical control data on the incidences of liver tumors in CD-1 mice. Evaluation of these comments resulted in no change in data gap status. No worksheet was done. See response dated 3/9/93 (S. Morris).

50248-229; 118530;
50248-229; 118533: These documents contain statistical analyses of male liver tumor incidences in the study at DPR doc. # 50248-222, rec. # 112345. Evaluation of these analyses resulted in no change in data gap status. No worksheet was done. See response

dated 3/9/93 (S. Morris).

50248-238; 123256: This document contained no new rationale or data. Evaluation of this material resulted in no change in data gap status. No worksheet was done. See response dated 10/13/95 (S. Morris).

50248-274; 144699: This document contains statistical analyses of male liver tumor incidences and male and female survival in the study at DPR doc. # 50248-222, rec. # 112345. Evaluation of these analyses resulted in no change in data gap status. No worksheet was done. See response dated 3/5/96 (S. Morris).

REPRODUCTION, RAT

**** 50248-246; 129439;** "Reproductive Effects of SBP-1382* (Resmethrin) Technical Administered Orally Via the Diet to Crl:CD*BR VAF/Plus* Rats for Two Generations with Two Litters per Generation", Study No. RBT-92-102; A.M. Hoberman; Argus Research Laboratories, Inc., Horsham, PA; 2/1/94. Groups of 30 Crl:CD*BR VAF/Plus* rats/sex/dose were continuously fed diets containing resmethrin (SBP-1382*, lot IN-0198-B3, 86.3% stated purity) at 0, 250, 500, and 1000 ppm through 2 generations (F0, F1) with 2 litters/generation (F1a, F1b, F2a, F2b). The FO's were exposed for at least 80 days then through mating, gestation, delivery of the F1a litter, a 21-day lactation period, weaning and sacrifice of F1a pups, a 26-day rest period, a second mating, sacrifice of F0 males, gestation, delivery of the F1b litter, a 21-day lactation period, weaning of F1b pups, and sacrifice of F0 females and non- selected F1b pups. The F2 generation was made up of selected F1b pups that were exposed, mated and sacrificed similarly to the F0 generation producing the F2a and F2b litters except all F2b pups were sacrificed 21 days post partum. There were no treatment-related effects on food consumption, body weight, clinical observations, gross pathology, histopathology, mating performance, or fecundity. A **possible adverse effect** was indicated by treatment-related effects seen at 1000 ppm: decreased pup viability in the F1a, F1b, F2a and F2b litters; transient decrease in body weight gain of both F1b sexes; increased mortality (2/30) in F1 adult males; decreased fertility for the F2b mating; and decreased feed consumption by F0 females while nursing smaller F1a litters (NOEL = 500 ppm). The study was unacceptable (S. Morris and J. Gee, 2/21/95) but upgraded to acceptable by submission of an adequate certificate of purity for the test material (S. Morris and J. Gee, 10/13/95).

50248-272; 139572: This document contained an adequate certificate of purity. Evaluation of these data resulted in a study status changed from "unacceptable, possible adverse effect" to "acceptable, possible adverse effect". A worksheet was done (S. Morris, 10/13/95).

50248-182; 054080; "The Evaluation of the Effects of SBP-1382 Following Dietary Administration Through Three Generations in Sprague-Dawley Rats" (Food and Drug Research Laboratories, Waverly Research Center, Laboratory No. 5739, 7/13/79) Resmethrin (SBP-1382 Technical, Lot No. 8176-RT, 90% purity) at 0, 500, 800, or 1250 ppm in the diet to 20 rats/sex/group for 3 generations; No chronic toxicity; **POSSIBLE ADVERSE EFFECT**-reduced litter size, litter weights, pup survival, pup weights and, increased pups cast dead; NOEL < 500 ppm; **UNACCEPTABLE**-a NOEL cannot be set because toxicity was found in all treated groups, diet analyses showed variable and often low recovery, the mating protocol was inadequate, necropsies were limited, no histopathology was done. Davis, 8/18/87.

EPA ONE LINER-NOEL < 500 ppm (LDT). Increased numbers of pups cast dead and decreases in pup weights at 21 days.

50248-202; 069528: This document contains the feed analysis of the study at DPR doc. # 50248-182, rec. # 054080. No worksheet was done (S. Morris 09/01/89).

50248-202; 069529: This document contained an acceptable retrospective diet analysis that demonstrated the homogeneity and stability of SBP-1382 technical in animal feed. This study was not sufficient to address the low recovery in diet analysis in the study at DPR doc. # 50248-182, rec. # 054080. A worksheet was done (Shimer/S. Morris, 09/01/89).

50248-182; 069531: This document contains statistical analyses of the findings of study at DPR doc. # 50248-182, rec. # 054080. No worksheet was done (S. Morris 09/01/89).

50248-083; 076009: This document contains EPA's evaluation of the study at DPR doc. # 50248-182, rec. # 054080. Examination of this evaluation data did not result in a change of study status. No worksheet was done (S. Morris, 10/04/89).

50248-184; 054439; "The Evaluation of SBP-1382 Following Dietary Administration Through One Generation in Sprague-Dawley Rats" 834 (Food and Drug Research Laboratories, Waverly Research Center, Laboratory No. 5458, 7/10/78) Resmethrin (SBP-1382 Technical, Lot No. 8176-RT, 90% purity) at 0, 500, 2500, or 5000 ppm in the diet to 20 rats/sex/group for one generation; Chronic toxicity NOEL = 2500 ppm (tremors, probable decreased body weight gains in males); **POSSIBLE ADVERSE EFFECT**-reduced gestation index, litter size, pup survival, pup weights and, increased stillbirths; Reproductive toxicity NOEL < 500 ppm; **UNACCEPTABLE**-not an SB950 study; some data are "estimated" or "assumed". Davis, 8/21/87.

EPA ONE LINER-NOEL < 500 ppm-increases in numbers of pups cast dead. At 2500 ppm increased pups cast dead and lower pup weight among survivors.

TERATOLOGY, RAT

** 50248-065; 007353; "Teratologic Evaluation of SBP-1382 Technical in the Albino Rat" Snell project # 2054-066; Booz, Allen & Hamilton Inc.; 11/26/79; resmethrin, SBP-1382 technical, Lot # 9037-RB, 86% purity. Groups of 25 pregnant rats were dosed by gavage with 0, 20, 40, or 80 mg/kg on gestation days 6-15 and sacrificed on day 20. Reduced food consumption and weight gain in dams and delayed ossification in fetuses were seen at 80 mg/kg. <u>No adverse effect</u> was indicated because maternal NOEL = fetal NOEL (40 mg/kg). The study status was changed from unacceptable (Davis, 8/12/87) to acceptable (S. Morris 9/14/89).

EPA ONE LINER-Teratogenic NOEL > 80 mg/kg (HDT)
Fetotoxic NOEL = 40 mg/kg
Fetotoxic LEL = 80 mg/kg (delay in skeletal development)
CORE Grade Guideline

50248-066; 007354: These documents contain appendices to 50248-065; 007353.

50248-200; 069524; This document contains a retrospective analysis of the stability of corn-oil solutions of the test material and historical data for reproductive performance

and spontaneous fetal abnormalities in Charles River CD rats. These data and the registrant's response (DPR doc. 50248-200, letter dated 07/30/89) sufficiently address the deficiencies in dosing-solution analysis, disease, number of litters, skeletal examinations, and historical control data in the study at DPR doc. # 50248-065, rec. # 007353. Evaluation of these data resulted in a change of study status. A worksheet was done (S. Morris, 09/14/89)

50248-200; 069525;
50248-201; 069525; This document contains a copy of the study at DPR doc. # 50248-065, rec. # 007353. No worksheet was done (S. Morris, 9/14/89).

50248-142; 956683; "Toxicological Evaluation of Pyrethroid Insecticide (5-Benzyl-3-Furyl) Methyl-2,2-Dimethyl-3-(2-Methylpropenyl) Cyclopropane-carboxylate (Resmethrin)" (U.S. Army Environmental Hygiene Agency, Study No. 51-0830-77. 5/16/77) (833-teratology in rats) Resmethrin (technical, 88% purity) at 0, 188, or 1500 mg/kg/day in the diet to groups of 30 females on days 6-16 of gestation with sacrifice on day 20 of 20/group; 10/group allowed full term pregnancies; **NO ADVERSE EFFECT**-Maternal NOEL (two deaths, tremors, and decreased food and water consumption) = Developmental NOEL (total litter resorption [15/30 dams] and lower pup birth weights) = 188 mg/kg/day; **UNACCEPTABLE**-only two dose levels, inadequate number of fetuses examined for visceral and skeletal anomalies. Davis 9/21/87.

50248-142; 058992: This document contains brief summary of the study at DPR doc. # 50248-142, rec. # 956683. No worksheet was done (S. Morris 11/1/89).

50248-142; 956682; "Toxicological Evaluation of Pyrethroid Insecticide (5-Benzyl-3-Furyl) Methyl-2,2-Dimethyl-3-(2-Methylpropenyl) Cyclopropane-carboxylate (SBP-1382^{TM})" (U.S. Army Environmental Hygiene Agency, Study No. 51-127-71/72. Undated) (833-teratology in rats) Resmethrin (technical, no purity given) by inhalation, intraperitoneal, or intragastric methods at various doses to various numbers of pregnant females; **NO ADVERSE EFFECT REPORTED**; NOEL cannot be established from the information given; **UNACCEPTABLE**-this is a few selected pages from one or more reports. Davis 9/22/87.

50248-164; 956681; "Degradation, Metabolism and Toxicity of Synthetic Pyrethroids" (Research Department, Sumitomo Chemical Co. 4/76) (833, 821, 842, 844) This journal article by J. Miyamoto (Environmental Health Perspectives 14: 15-28, 1976) reviews the toxicity of resmethrin, among several synthetic pyrethroids. **POSSIBLE ADVERSE EFFECT**-increased liver weights and histopathological liver changes in rats for all compounds, including resmethrin (24 week feeding study); no developmental toxicity or genotoxicity reported. **UNACCEPTABLE**-review article, not a study. Davis 9/18/87.

TERATOLOGY, RABBIT

50248-064; 007352; "Teratologic Evaluation of SBP-1382 Technical in Albino Rabbits", FDRL # 6288; Food and Drug Research Laboratories, Waverly Research Center; 10/31/79; resmethrin, SBP-1382 technical, 90% purity; Groups of 20 pregnant rabbits were dosed by gavage with 0, 10, 30, or 100 mg/kg on gestation days 6-18 and sacrificed on day 29. There were no treatment-related maternal effects. Treatment-related reproductive/developmental effects were increased extra sternebrae at 100 mg/kg and increased resorptions, dark livers, and fused sternebrae at 10, 30, and 100 mg/kg. A possible adverse effect is indicated because the

reproductive/developmental effects occurred in the absence of maternal toxicity. The study is unacceptable and not upgradeable because a NOEL was not demonstrated for the reproductive/ developmental effects (Davis, 8/11/87; S. Morris, 11/1/89).

EPA ONE LINER-NOEL $\geq$ 100 mg/kg (highest level tested). Core Grade minimum.

50248-201; 069524; This document contains a retrospective analysis of the stability of corn-oil solutions of the test material. These data sufficiently address the deficiencies in dosing-solution analysis in the study at DPR doc. # 50248-064, rec. # 007352. Evaluation of this study did not result in a change of study status. No worksheet was done (S. Morris, 09/14/89)

50248-201; 069527; This document contains retabulations of raw data. Evaluation of these data did not result in a change of study status. A supplemental worksheet was done (S. Morris 09/14/89).

50248-142; 956684; "Rabbit Teratogenic Study" (Industrial Bio-Test Laboratories, Inc., Number J5579 3/8/68) This study was determined to be Invalid by the EPA (July, 1983). DPR did not review it.

50248-142; 055513; "Rabbit Teratogenic Study" (Industrial Bio-Test Laboratories, Inc., Number J6146, 7/22/68) This study was determined to be Invalid by the EPA (July, 1983). DPR did not review it.

**** 50248-218; 096696;** "Developmental Toxicology (Embryo-Fetal Toxicity and Teratogenic Potential) Study of SBP-1382* (Resmethrin) Technical Administered Orally Via Stomach Tube to New Zealand White Rabbits"; Project ID ARGUS 718-003; A.M. Hoberman; Argus Research Laboratories, Inc., Horsham, PA; 3/13/91. Groups of 18 pregnant New Zealand White [Hra:(NZW)SPF] rabbits were dosed by oral gavage with suspensions of resmethrin (SBP-1382*, lot 8N0731B3, 87% stated purity, corn oil vehicle) at 0 (vehicle), 0 (sham), 30, 120, or 300 mg/kg/day (corrected for purity) on gestation days 6 through 18 and sacrificed on day 29. The dams were subjected to gross necropsy of the thoracic and abdominal viscera and detailed necropsy of the reproductive organs. External, visceral, and skeletal examinations were performed on all fetuses. There were no significant maternal effects (maternal NOEL $\geq$ 300 mg/kg/day. A **possible adverse effect** was indicated at 300 mg/kg/day where 5/17 litters aborted and 2/17 were completely resorbed (developmental NOEL = 120 mg/kg/day). No fetal visceral or skeletal abnormalities were reported. The study was acceptable (S. Morris and J. Gee, 2/7/92).

TERATOLOGY, MOUSE

58248-142; 956685; "Teratogenic Study of SBP-1382. White Mice" (Industrial Bio-Test Laboratories, Inc., Number P6178, 7/15/68) This study was determined to be Invalid by the EPA (July, 1983). DPR did not review it.

GENE MUTATION

** 50248-199; 066410; "Salmonella/Mammalian-Microsome Plate Incorporation Mutagenicity Assay (Ames Test) With A Confirmatory Assay" (Microbiological Associates Inc., Study Number T5747.501014, 12/30/87) Triplicate plates of Salmonella typhimurium strains TA98, TA100, TA1535, TA1537, TA1538 were exposed to Resmethrin NRDC 104 (Lot No. 6L0762, 90.5% purity) at 10000, 6667, 3333, 1000, 667, and 0 ug/plate, with and without activation. A confirmatory assay was done. **NO ADVERSE EFFECT**-No evidence of mutagenicity was found. **ACCEPTABLE.** Davis 6/2/88

50248-142; 956687;"Mutagenicity Evaluation of SBP-1382 Technical" (Litton Bionetics, Inc. Project No. 2683, 4/77) 842-Gene Mutation. Resmethrin (purity unknown) at 0, 0.001, 0.010, 0.100, 1.000, 5.000 ul/plate ± activation in Ames assay with Salmonella typhimurium strains TA98, TA100, TA1535, TA1537, TA1538 and in Saccharomyces cerevisiae strain D4 assay; DMSO solvent control; **NO MUTAGENICITY, UNACCEPTABLE**-insufficient information about test material, single plates, no confirmatory repeat assay. Davis, 9/18/87.

50248-142; 058992; "Toxicological evaluation of pyrethroid insecticide (5-benzyl-3-furyl) methyl-2,2-dimethyl-3-(2-methylpropenyl) cyclopropanecarboxylate (resmethrin)" study # 51-0830-77; U.S. Army Environmental Hygiene Agency; 1/77; This document contained a brief summary of a bacterial mutagenicity study. No adverse effect was indicated. No worksheet was done (S. Morris, 11/1/89).

CHROMOSOME MUTATION

** 50248-199; 066411; "Chromosome Aberrations in Chinese Hamster Ovary (CHO) Cells" (Microbiological Associates Inc., Study Number T5747.337003, 3/8/88) Duplicate plates of CHO cells were exposed to Resmethrin NRDC 104 (Lot No. 6L0762, 90.5% purity) at 0, 40, 80, 160, or 320 ug/ml in the absence of activation and 0, 30, 60, 120, or 240 ug/ml with duplicate flasks in the presence of activation. 100 cells/flask were scored for chromosome aberrations. **NO ADVERSE EFFECT**-No evidence of mutagenicity was found. **ACCEPTABLE.** Davis 6/2/88

DNA DAMAGE

** 50248-199; 066409; "Unscheduled DNA Synthesis in Rat Primary Hepatocytes" (Microbiological Associates Inc., Study Number T5747.380, 1/15/88) Triplicate cultures of primary rat hepatocytes were exposed to Resmethrin NRDC 104 (Lot No. 6L0762, 90.5% purity) at 1000, 500, 250, 100, 25, 10, 2.5, 1.0, 0.25, 0.1, 0 ug/ml, but the highest four dose levels were not evaluated for unscheduled DNA synthesis because of cytotoxicity. 50 cells per culture were scored for all other dose levels and for positive and negative control groups. **NO ADVERSE EFFECT**-No evidence of DNA damage was found. **ACCEPTABLE.** Davis 6/2/88

NEUROTOXICITY

No study submitted or required at this time.

SUPPLEMENTAL INFORMATION

50248-213; 086959; "Two-generation reproduction toxicity study in rats by dietary mixture administration", study no. 2059; M.H. Savary; Centre International de Toxicologie, Miserey, France; 07/26/89; bioresmethrin, .95%. This was a two generation (F0, F1) study with one litter (F1, F2) per generation. Dietary exposures were 0, 80, 250, 750, or 2250 ppm. Twenty-five F0 rats / sex / group were exposed for 8 weeks then paired. Exposures continued through pregnancy and lactation. One F1 pup / sex / litter / group were exposed for 14 weeks then paired. Exposures continued through pregnancy and lactation. Treatment-related effects in adults were decreased body weights at 750 and 2250 ppm and mild liver effects (paleness, accentuated lobular pattern, microscopic steatosis) in females at 250 and 2250 ppm and both sexes at 750 ppm (parental NOEL = 80 ppm). Treatment-related reproductive effects were decreased body weights in pups at 750 ppm and a **possible adverse effect** was indicated by uterine degeneration at 750 and 2250 ppm and pup mortality being increased at 750 ppm and total at 2250 (reproductive NOEL = 250 ppm). The study is unacceptable and not upgradeable because the registered active ingredient was not used (S. Morris, 2/6/91).

NOTE: Resmethrin is a mixture of bioresmethrin and cismethrin.

50248-083; 076009;
50248-222; 112340;
50248-222; 112343: These documents contain EPA one-liners and evaluations.

50248-212; 086958: This document contains the World Health Organization's Environmental Health Criteria (1989, 79 pages) and Health and Safety Guide (1989, 30 pages) for resmethrins.

50248-229; 118424;
50248-229; 118437;
50248-229; 118438;
50248-229; 118439;
50248-229; 118444: These documents contain articles from the open literature related to the toxicokinetics of the test material and rodent liver pathology. No worksheets were done (S. Morris, 2/9/93).

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50248-229 118530
50248-229 118533
50248-238 123256
50248-245 128007
50248-246 129439
50248-252 134161
50248-272 139572
50248-274 144699
50248-275 150992
50248-164 956681

These records were not reviewed because the documents were not in the listed volumes:

50248-047 058289
50248-047 960762

These records are on file but no yet reviewed:

50248-245 128007
50248-252 134161